

## Do C-reactive protein and procalcitonin predict hospital-acquired infection in patients with trauma?

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Trauma patients frequently present signs of sepsis such as fever, tachycardia, hyperventilation and leukocytosis even in the absence of infection. The diagnosis of infection in patients with trauma is essential for correct patient management. However, over utilization of antibiotics can lead to the emergence of multiresistant organisms, increased toxicity, and increased cost. The C-reactive protein (CRP) is currently the most widely used parameter to support the diagnosis of infection. As routine laboratory tests often provide inadequate discrimination in the diagnosis of infection in patients with trauma, there is a need for inflammatory agents that are reliable enough to differentiate hospital-acquired infections (HAI) from other types of inflammation both requiring different forms of therapy. In adults and children, infection, and sepsis have been found to be associated with increased serum levels of calcitonin precursors. Procalcitonin (PCT) concentrations are very low in healthy individuals, but have been shown to increase markedly after endotoxin administration during severe systemic infection and septic shock.<sup>1</sup> In this regard, we designed a prospective study to define the value of PCT and CRP concentrations and white blood cell (WBC) count in the diagnosis of HAI in patients with trauma admitted to the surgical intensive care unit (ICU).

The study included 41 consecutive adult patients with trauma admitted to emergency surgical ICU at Istanbul University, Istanbul Medical Faculty Hospital, Turkey. All of the patients' age, gender, type of trauma, glasgow coma score (GCS), Acute Physiologic Assessment and Chronic Health Evaluation (APACHE) II Score, and Sequential Organ Failure Assessment (SOFA) score were recorded. All patients were examined for signs and symptoms of infection at the time of admission and daily thereafter by an infectious diseases consultant, and the diagnosis of an HAI was made according to the criteria defined by the Centers for Diseases Control and Prevention. Informed consent was obtained from all patients. Infected patients at the time of admission to ICU, patients with penetrated abdominal trauma, patients who underwent recent abdominal surgery

**Table 1** - The comparison of the markers of infection in the infected group.

Marker	Initial value* (n=21)	Latter value† (n=21)	P-value
WBC count (/mm <sup>3</sup> )	13109.5	13432.9	0.794
CRP concentration (mg/L)	49.4	167.2	<0.001
PCT concentration (ng/mL)	6.2	4.7	0.106

WBC - white blood cell, CRP - C-reactive protein, PCT - procalcitonin, \*The values obtained from the infected group at the time of admission to intensive care unit, †The values obtained from the infected group at the onset of hospital-acquired infections

were excluded from the study. Venous blood samples were obtained for measurement of serum concentrations of PCT, CRP and WBC count, at the time of admission to ICU (initial), and at the onset of HAI (latter). The PCT concentration was measured by immunoluminometric assay with the commercially available Lumitest® PCT (BRAHMS Diagnostica GmbH, Berlin, Germany). The CRP was measured by immunoturbidimetry with the Turbiquant® CRP test kit (Dade Behring, Marburg, Germany). The normal values for PCT concentrations is 0 - 0.5 ng/ml, for CRP concentrations is 0 - 5 mg/L, and WBC count is 4000 - 9000/mm<sup>3</sup>. Results are expressed as mean ( $\pm$  SD). Mann Whitney U test was used in univariate analysis of independent samples. For paired analysis, Wilcoxon test was used,  $p < 0.05$  was accepted as the level of significance.

There were 34 male (83%) and 7 female (17%) patients and had the following clinical and laboratory findings at admission to ICU: mean age  $\pm$  SD was 39.8  $\pm$  19.7 years, mean APACHE II score  $\pm$  SD was 12.8  $\pm$  7.1 points, mean GCS  $\pm$  SD was 10.9  $\pm$  4.1 points, mean SOFA score  $\pm$  SD was 5  $\pm$  2.6 points, mean WBC count  $\pm$  SD was 14521.5  $\pm$  6043.2/mm<sup>3</sup>, mean CRP concentration  $\pm$  SD was 54.1  $\pm$  45.4 mg/L, mean PCT concentration  $\pm$  SD was 4.6  $\pm$  1 ng/mL. Thirteen patients had only head trauma while 3 patients had only abdomen, one patient only chest, and one patient only extremity trauma. The rest of the patients (n=23) had multi-trauma at admission to ICU. Hospital-acquired infections were diagnosed in 21 (51%) patients. Mean date of infection diagnosis  $\pm$  SD was 6.6  $\pm$  3.5 days. Among infected patients, ventilator associated pneumonia was diagnosed in 12 (29.1%) patients, bacteremia in 3 (7.3%), catheter-related

infection in 2 (4.9%), meningitis in 2 (4.9%), intra-abdominal abscess in 1 (2.4%), and pyelonephritis in 1 (2.4%) patient. Among the initial findings of all patients' age, gender, APACHE II score, GCS, SOFA score, WBC count, CRP and PCT concentrations were not significantly different between the infected and non-infected groups. The initial CRP and PCT concentrations and WBC count and the values obtained at the onset of HAI in the infected group were listed in **Table 1**. Only serum CRP concentrations obtained at the onset of HAI increased significantly compared with the initial values in the infected group ( $p < 0.001$ ). The recognition of HAI in trauma patients is difficult as no single marker of inflammation allows the establishment of the diagnosis. In this regard, we prospectively investigated the benefit of a new innovative marker PCT and a conventional marker CRP together with WBC in diagnosis of HAI in patients with trauma admitted to a surgical ICU.

The mean PCT values at admission to ICU were 4.62 ng/ml, CRP values were 54.14 mg/L, and WBC values were 13521.46/mm<sup>3</sup>, and all those were above the reference ranges. Early elevation of PCT and CRP concentrations and WBC count may be related to tissue damage after trauma. Wanner et al,<sup>2</sup> pointed out that mechanical trauma causes elevated PCT levels depending on the severity of the injury. Levels were in the peak on day 1 to 3 and fall thereafter. The PCT is a sensitive marker of sepsis and severe multiple organ dysfunction syndrome in injured patients. Routine PCT analysis appears to be useful in the early recognition of post-traumatic complications. A secondary rise in PCT appears to indicate superadded bacterial sepsis. On the other hand, in our study, there were no significant differences between the initial and the latter PCT concentrations and WBC counts in the infected group while the difference for CRP was statistically significant. It is clear that early diagnosis of HAI prevents the development of sepsis. There were only 3 bacteremias patients in our study. In these patients, CRP exhibited an increase but not PCT except in one bacteremic patient and only this patient met all sepsis criteria. We evaluated the course of PCT and CRP concentrations and WBC counts in the infected group and took their initial values as the control group. Our aim was to diagnose HAI at the very early stages of the infection. So, these tests were not repeated in the non-infected group. It is possible that in the infected group, PCT levels had began to rise by the time the initial levels were taken and had began to fall by the time the latter levels were taken. This will explain why the initial PCT levels were higher (nearly reaching statistical significance) in the infected than in the non-infected group and why the

PCT levels were higher on the initial sample than on the latter. In our study, CRP assessment has proven more helpful in the prediction of HAI compared with PCT and WBC counts. Miller et al<sup>3</sup> reported that CRP but not WBC is useful in determining the presence of infection in trauma patients. In a study performed by Ugarte et al<sup>4</sup> it was reported that CRP remains to be the best discriminant test due to its good sensitivity and specificity, and could discriminate between infected and non-infected patients. They recommended that PCT should not replace CRP as a marker of infection in ICU patients, but the combination of both parameters can indicate the presence of infection with greater specificity. There had been similar results in a study performed by Mimoz et al.<sup>5</sup> They evaluated 21 blunt trauma patients and found that at the late post-traumatic period (day 7) while CRP concentrations remain elevated in all patients, PCT concentrations were only raised in septic patients. Recently a meta-analysis was performed by Simon et al.<sup>6</sup> This analysis included 12 published studies that evaluated PCT and CRP for the diagnosis of bacterial infection in hospitalized patients. They concluded that the overall accuracy of PCT markers is higher than that of CRP markers to differentiate bacterial infections from other non-infective causes of systemic inflammation. They evaluated a heterogeneous patient population with different age groups with different types of infections from different areas of the hospitals unlike our study group.

Sepsis may lead to a lethal multiple organ failure in trauma patients, especially in cases of delayed diagnosis of infection. Together with the clinical symptoms, CRP is a useful marker for the rapid identification of HAI in patients with trauma.

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## Scolicidal agents in hydatid cyst surgery

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Surgical operation is the treatment of choice for patients with hydatid cyst as chemotherapy is still controversial. Inoculation of a scolicidal agent into the cavity of hydatid cyst to reduce the risk of spillage of viable protoscolices is a major part of the surgical technique. Although numerous scolicidal agents have been used for many years, good evidence for their efficacy in vivo is lacking. Therefore, the effectiveness of some of these agents needs to be tested.

Fresh, fertile hydatid cysts from the liver were obtained shortly after surgical removal in Basrah General Hospital, Basrah, Iraq. The material was allowed to settle in a sterile bottle, and the supernatant was removed. The viability of protoscolices was determined by flame cell activity and vital staining with 1% eosin. Viable scolices show flame cell activity and do not take up the dye.<sup>1</sup> The test was carried out on 5 samples. The scolicidal agents examined were hypertonic solution 30%, normal saline 0.9%, betadine, ethyl alcohol 70% and 95%. Two ml of each scolicidal were placed in a test tubes. A drop of protoscolex rich sediment was added to each tube and was mixed gently. Following 5, 10 and 30 minutes of exposure, the viability of the protoscolices was determined microscopically by assessing flame cell activity and lack of vital staining with 1% eosin.

Betadine, hypertonic solution 30% and ethyl alcohol 95% were effective in killing the protoscolices within 5-10 minutes time. In contrast, saline solution 0.9%, and ethyl alcohol 70% could not show any lethal effect on the protoscolices even after 30 minutes time. Cyst fluid contains thousands of protoscolices and each one has the potential to grow into a new hydatid cyst. Thus, it has been traditional to inject scolicidal agents into the unopened hydatid cyst due to the risk of spillage into the peritoneal cavity leading to recurrent disease. Hypertonic solutions 30% have become the scolicidal agents of choice over the past years. Although Besim<sup>2</sup> demonstrated that 5% saline have no effect on scolices, many surgeons recommended the use of 3% saline.<sup>3,4</sup> Our findings prove that there is no scolicidal effect (100%) can be shown with 20% saline at 5 minutes.<sup>2</sup> But, it should not be used in patients who have cysts connecting with the biliary tree due to the danger of sclerosing cholangitis.<sup>5</sup>

Betadine is an effective scolicidal agent, as demonstrated in this study, but polyvinylpyrrolidone storage disease, renal shut down, sterile peritonitis and sclerosing serositis are the associated complications and its use is restricted to preoperative local antiseptics of intact adult skin.<sup>6</sup> Ethyl alcohol is an effective agent at a concentration of 95%. Unfortunately, it can cause caustic damage to the epithelium of communicating bile ducts leading to sclerosing cholangitis and it is strongly concentration dependent,<sup>2,3,6</sup> as observed in this study. Therefore, the surgeon in practice in our hospitals aspirates the cyst fluid first. If the aspirate is clear, then they would use any effective scolicidal agents without hazard. However, if the aspirate is yellow in color it means there is a biliary communication. So, the risk of sclerosing cholangitis may be the problem of using a certain agent. Therefore, total evacuation and prevention of any contact of germinative membrane with the peritoneal surface are essential as the germinative membrane can contain viable protoscolices despite proper cyst fluid inactivation.

In conclusion, the risk of dissemination of the cyst contents can be avoided by injecting a potent scolicidal agent, which is an important step in hydatid cyst surgery. The best scolicidal agent to be used is betadine. However, experiment in vitro and in vivo results need to be studied further.

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